

some beverage alcohols. The lethal concentration in the blood is the same for all we have tested, but there is considerable difference as between alcohol from various sources in the dose required to produce this concentration, a fact suggesting a difference in the rate of oxidation.

Our observation that the concentration of blood sugar influences the pharmacological effects of alcohol may offer some explanation of the alleged idiosyncrasies in human reactions to alcohol. It affords a new factor that must be taken into consideration in any experimental study of the pharmacology of alcohol. Our technique of determining doses under conditions of equilibrium affords a method of making precise quantitative measurement of the toxicity of alcohols from various sources.

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### THE OPERCULAR APPROACH TO THE PITUITARY<sup>1</sup>

SURGICAL techniques for the removal of the pituitary gland of teleosts have been described by Parker<sup>2</sup> in the catfish, *Ameiurus*, and by Matthews<sup>3</sup> in the killifish, *Fundulus*. These techniques are not quite satisfactory in experiments to be carried on over long periods of time, inasmuch as the operated animals survived only for a short time; the catfish surviving only two days, and the killifish several weeks. A new approach to the teleost hypophysis whereby tissue injury is reduced to a minimum has been worked out by the author with more satisfactory results.

#### (1) THE CATFISH

Parker's method of hypophysectomy consisted in making a U-shaped cut through the gular membrane from the opercular opening on one side to that on the opposite side of the animal, so that the lower jaw was completely separated from the gills. Having accomplished this initial opening, the operation was completed by puncturing a hole in the parasphenoid and snipping off the gland. This method involves a two-inch incision which may be avoided in the following manner. The catfish is wrapped in a wet cloth and placed on its back under a binocular microscope. The mouth is held open by five retractors, and an incision about two to three millimeters in length is made through the mucous membrane covering the parasphenoid bone. A trephine drill is then introduced under the operculum and between the first and second gill arches. One merely lifts the operculum and gently separates the first from the second gill arch. This

procedure exposes a wide natural cavity, and the drill may now be inserted directly perpendicular to the roof of the mouth. The hypophysis can be seen through the bone as a small yellow spot. A hole (1.5 mm in diameter) is drilled through the bone, the gland sucked up in a pipette, and the wound closed by a single suture through the mucous membrane. The operation can be performed virtually without the loss of a single drop of blood and need not take over three minutes. The animal is returned to a tank of running tap water and survives for many months. Within a week, the suture disappears and the cut membrane heals over completely.

#### • (2) THE KILLIFISH

Matthews's method of hypophysectomy involved a sub-oral route, since he first made a V-shaped incision through the branchiostegal membrane with the base of the V at the tip of the tongue. The tongue was then pulled sufficiently ventral to expose the region of the pituitary. My operations with the sub-oral route proved unsatisfactory mainly because of the size of the initial incision, and the necessary cutting of a large blood vessel running along the ventral surface of the lower jaw. These two difficulties may be avoided by the opercular approach. The fish, first immobilized by immersion in cracked ice, is placed on its left side under an operating microscope. The operculum is elevated and held by a single retractor. The first and second gill arches are separated, thus exposing a wide space directly below which the hypophysis is located. A three-millimeter incision is made through the epithelial membrane slightly lateral to the mid-line in order to avoid a median artery. A hole is drilled with a trephine drill (1 mm in diameter) and the gland sucked up in a pipette. The wound is not closed by a suture because of the proximity of the median artery, but the circular piece of bone excised by the drill may be replaced to close the wound. The operation may be performed within five minutes and if done with sufficient care is a totally bloodless operation. The animal is placed in salt water for a day and then transferred to running tap water, as Matthews recommends, or it may be placed directly in tap water at room temperature.

This approach to the pituitary gland under the operculum and between the first and second gill arches may prove satisfactory for other teleost fishes.<sup>4</sup>

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<sup>2</sup> G. H. Parker, *Jour. Exp. Zool.*, 69: 199, 1934.

<sup>3</sup> S. A. Matthews, *Biol. Bull.*, 64: 315, 1933.

<sup>4</sup> Smith, Burr and Ferguson (*Endocrin.*, 19: 409, 1935), describe an orbital approach for hypophysectomy in the goldfish. These authors state, however, that their operative procedure involves enucleation of the right eye, severe traumatization of the interorbital plates, invariable rupture of an artery, blind groping for the hypophysis, traumatization of the hypothalamus and successful extirpation in one of seventeen cases.